SUMMARY

1. A determination has been made of the indices of the constants of relative acidity (pK_a) of 13 anthraquinones in water, methanol, acetone, dimethylformamide, and dimethyl sulfoxide.

2. Linear equations of the relationship between $pK_a^{H_2O}$ and pK_a in acetone, dimethylformamide, and dimethyl sulfoxide have been derived.

3. The indices of the titration constants (pK_t) have been calculated, and these have enabled it to be shown that the optimum conditions for the titration of the anthraquinones are achieved in dimethyl sulfoxide.

LITERATURE CITED

1. V. A. Stikhin and A. I. Ban'kovskii, in: The Search for and Chemical Study of Biologically Active Substances [in Russian], Moscow, No. 6 (1973), pp. 124-237.
2. A. S. Romanova, in: Medicinal Plants [in Russian], Moscow, Vol. 15 (1969), pp. 538-555.
3. V. P. Georgievskii, N. A. Kazarinov, and M. O. Karryev, Physicochemical Methods of Analyzing Biologically Active Substances of Plant Origin [in Russian], Ashkhabad (1976), pp. 216-218.
4. É. P. Kemertelidze and V. P. Georgievskii, Physicochemical Methods of Analyzing Some Biologically Active Substances of Plant Origin [in Russian], Tbilisi (1977), pp. 198-217.
5. N. A. Izmailov and I. F. Zabara, in: Collection of Papers on Physical Chemistry [in Russian], Moscow–Leningrad (1947), pp. 310-328.
6. V. É. Umanskii and A. V. Luzanov, in: Computer Mathematics and Computer Technique [in Russian], Kharkov, No. 5 (1974), pp. 10-12.
7. A. V. Luzanov and V. É. Umanskii, Opt. Spektrosk., 39, No. 5, 816 (1975).
8. A. J. Gordon and R. A. Ford, The Chemist's Companion, Wiley-Interscience, New York (1972)
9. B. Pullman and A. Pullman, Quantum Biochemistry, Wiley, New York (1963).
10. D. N. Shigorin and N. S. Dokunikhin, Zh. Fiz. Khim., 29, 1958 (1965).
11. I. P. Kovalev and E. P. Titov, The Infrared Absorption Spectra of Some Groups of Natural Compounds [in Russian], Kharkov (1966).
12. D. N. Shigorin and N. S. Dokunikhin, Dokl. Akad. Nauk SSSR, 100, No. 2, 323 (1958).
13. I. Gyenes, Titration in Nonaqueous Media, Van Nostrand, Princeton (1967).
14. L. N. Bykova and S. I. Petrov, Usp. Khim., 39, No. 9, 1631 (1970).

STEREOCHEMISTRY OF FESHURIN, NEVSKIN, AND COLLADOCIN

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The stereochemistry of feshurin has been suggested on the basis of passage to a substance with a known absolute configuration — conferol. It has been shown that feshurin and nevskin are isomers at the $C_{6'}$—OH. The configuration of nevskin has been determined. The absolute configuration of colladocin has been established by means of a study of the influence of the orientation of the hydroxy group at $C_{2'}$ in terpenoid coumarins of the samarcandin series on the chemical shifts of the $C_{1'}$—CH_2OAr.

Recently, by a comparative study of the signs of the specific rotations of the terpenoid coumarins we have established that the coumarins of the samarcandin series with a negative sign of the rotation have the axial orientation of the methyl group at $C_{2'}$ and we have deter-

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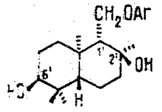
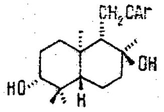
mined more accurately the orientation of the C_2'—CH_3 group in nevskin [1]. The absolute configurations of six coumarins and of their anhydro derivatives — samarcandin and isosamarcandin and their anhydro derivatives badrakemin and colladocin, and conferol and moschatol, respectively — were suggested simultaneously.

On the basis of the results of a comparison of the circular dichroism curves of the keto acids obtained from oleanolic acid and colladocin, which is an isomer of moschatol at the double bond, Piner and Rodriguez [2] have put forward an absolute configuration of colladocin with the trans-nonsteroid linkage of the biocyclofarnesane residue and with the —CH_2OAr substituent at C_1' in the equatorial position. Thus, two different pathways have led to the same result. Continuing this work, we have performed the following investigations.

The terpenoid coumarins feshurin (I) and nevskin (II), isolated from *Ferula schtschurovskyana* [3] and *F. nevskyi* [4] proved to be isomeric compounds with respect to the orientation of the hydroxy group at C_6', since when (I) and (II) were oxidized with chromium trioxide a ketone identical with nevskone was obtained [3, 5]. The relative configuration (II) has been put forward for nevskin on the basis of the results of a study of PMR spectra using paramagnetic shift reagents [4, 6]. Feshurin and nevskin have negative specific rotations. According to what has been reported previously, they must differ from the coumarins of the samarcandin series with a positive specific rotation only in the orientation of the methyl (hydroxy) group at C_2' [1]. To confirm this, we have compared the dehydration products of samarcandin (III) and ferushin (I). In actual fact, the two substances gave one and the same anhydro derivative — conferol (IV). Since the absolute configuration of the latter had been established previously [1], ferushin has configuration (I). Consequently, its isomer at C_6'—OH, nevskin, has the configuration IIa.



I



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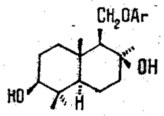

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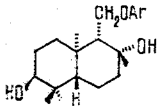

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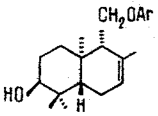

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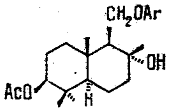

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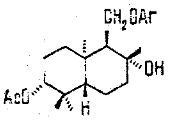

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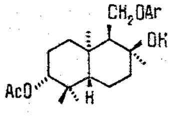

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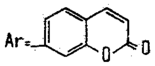

In a study of the stereochemistry of terpenoid coumarins of the samarcandin series (with a hydroxy group at C_2'), we directed our attention to the nonequivalence of the protons of the aryloxymethyl group —CH_2OAr at C_1'. We noted that the orientation of the tertiary hydroxy group affects the chemical shifts of the signals of the aryloxymethyl group in the spectra of the coumarins of this series. When the —CH_2OAr substituent at C_1' has the equatorial orientation, the distance between the center of the C_1'—CH_2 bond and of the hydroxy group at C_2' is practically independent of whether the latter has the axial or the equatorial orientation. Consequently, when the C_1'—CH_2OAr group has the equatorial orientation, the signals concerned must appear in the form of one-proton quartets, regardless of the orientation of the hydroxy group at C_2'. In actual fact, a comparison of the PMR spectra of samarcandin, isosamarcandin, feshurin, and nevskin confirms our conclusions. In the coumarins with an axial C_1'—CH_2OAr substituent the distance between the axial C_1'—CH_2OAr and C_2'—OH increases, and for these no influence of the hydroxy group on the chemical shifts of the protons of the aryloxymethyl group is observed.

An exception is deacetylkellerin, in the spectrum of which, although the C_1'—CH_2OAr and C_2'—OH groups are present in the trans-diaxial orientation, the protons of the aryloxymethyl group give two one-proton quartets [7, 8]. This is possibly explained by the fact that in the spectrum of kellerin the signal of the acetoxy group is observed in an anomalously strong field — at 1.71 ppm. The resonance of this group in such a strong field is due to the screening influence of the coumarin nucleus, which is possible only in the case of the axial orientation of the C_1'—CH_2OAr and C_6'—OH substituents [8]. In supplementation of what has been said above, it must be added that the signals of the gem-hydroxylic protons of ferucrin and deacetylkhellerin, which are isomeric at C_6'—OH, differ only by their half-width values and are observed at 3.15 ppm, although they are epimers. These facts give grounds for assuming that, with the axial orientation of the substituents at C_1' and C_6', an intramolecular hydrogen bond is possibly formed between the hydroxyl at C_6' at the carbonyl of the coumarin nucleus, leading to the above-mentioned anomalous values of the chemical shifts of the C_6'–H, C_6'-OAc, and C_1'–CH_2OAr groups. Anomalous chemical shifts of the C_6'–OAc and C_1'–CH_2OAr group are also observed in the spectra of the epimeric monocyclic terpenoid coumarins feropolin (C_6'-aOH) [9] and foliferin acetate (C_6'–eOH) [10].

In coumarins with an axial substituent at C_1' and an equatorial hydroxy group at C_2', because of the above-mentioned influence of the C_2'–OH group the protons of the C_1'–CH_2OAr group become nonequivalent and should appear in the form of two one-proton quartets.

The coumarin colladonin has been isolated previously from *Colladonia triquetra* and the relative configuration (V) has been proposed for it on the basis of chemical transformations and spectral characteristics [11]. By comparing the physicochemical constants of colladocin with those of nevskin acetate [6] and of isosamarcandin acetate, Borisov et al. [11] showed that these substances were not identical. They also differed from ferucrin acetate [12]. In view of the dependence of the sign of the specific rotation on the stereochemistry of terpenoid coumarins [1], it may be assumed that colladocin has the trans-nonsteroid linkage in the terpenoid part, and, as found previously [11], the methyl group at C_2' has the axial orientation. Consequently, the hydroxy group at C_2' has the equatorial orientation.

In the PMR spectrum of colladocin, the protons of the aryloxymethyl group give two one-proton quartets at 4.08 and 4.34 ppm (J_{gem} = 10.5, J_{vic} = 6 Hz) [11]. As shown above, such nonequivalence is observed only when C_1'–CH_2OAr and C_2'–OH are present in the cis position, i.e., with the axial orientation of C_1'–CH_2OAr and the equatorial orientation of C_2'–OH. Since substances with an equatorial –CH_2OAr substituent at C_1' and an equatorial –OH group at C_2' (nevskin and feshurin) are known, the only possible configuration remaining for colladocin is that with an axial –CH_2OAr group at C_1'. Thus, colladocin is an isomer at ferucrin acetate (VI) at the C_2'–OH group and for it we suggest the absolute configuration (Va).

It must be observed that in this series of coumarins no isomer of deacetylkellerin at the C_2'–OH group has yet been found.

SUMMARY

Absolute configurations of feshurin and nevskin are put forward on the basis of a passag to a substance of known configuration. The influence of a hydroxy group at C_2' in a terpenoi coumarin on the nonequivalence of the protons of the aryloxymethyl group has been shown and the absolute configuration of colladocin has been corrected.

LITERATURE CITED

1. A. I. Saidkhodzhaev and V. M. Malikov, Khim. Prir. Soedin., 707 (1978).
2. M. Pinar and B. Rodriguez, Phytochemistry, 16, No. 12, 1987 (1977).
3. A. Sh. Kadyrov, A. I. Saidkhodzhaev, and V. M. Malikov, Khim. Prir. Soedin., 228 (1979).
4. V. Yu. Bagirov and N. P. Kir'yalov, Khim. Prir. Soedin., 387 (1972).
5. V. Yu. Bagirov, Khim. Prir. Soedin., 652 (1978).
6. V. Yu. Bagirov, V. P. Sheichenko, and A. I. Ban'kovskii, Khim. Prir. Soedin., 450 (1976).
7. V. B. Andrianova, Yu. E. Sklyar, M. E. Perel'son, M. G. Pimenov, Khim. Prir. Soedin., 795 (1973).
8. M. E. Perel'son, V. I. Sheichenko, Yu. E. Sklyar, and V. B. Andrianova, Khim.-Farm. Zh., 8, 33 (1977).
9. T. Kh. Khasanov, A. I. Saidkhodzhaev, and G. K. Nikonov, Khim. Prir. Soedin., 91 (1976).
10. A. Sh. Kadyrov, A. I. Saidkhodzhaev, and V. M. Malikov, Khim. Prir. Soedin., 518 (1978).
11. V. N. Borisov, A. I. Ban'kovskii, N. S. Pavlova, L. Bubeva-Ivanova, V. I. Sheichenko, an V. S. Kabanov, Khim. Prir. Soedin., 247 (1973).
12. A. A. Nabiev, T. Kh. Khasanov, and V. M. Malikov, Khim. Prir. Soedin., 17 (1979).